

**REMARKS**

The pending office action addresses claims 16-33, claims 34-36 having been withdrawn as being directed to a non-elected invention. Currently, claims 16-33 stand rejected. By this response, Applicant has amended claims 16-19, 21, 22, and 29, and canceled claims 20 and 26-28. In particular, claim 16 is amended to recite the steps of selecting a first and second individual from the population, hybridizing the genomic DNA of each of the individuals to a reference microarray, determining the hybridization intensity ratio for each of the hybridized and non-hybridized segments of the microarray, then converting the ratio to a binary digit of 0 or 1 to produce a bit string of 0 or 1 bits for each individual. Each of the strings has the same total number of bits and each bit has a unique position common to both the strings. Finally, the relatedness of the strings is determined by comparing the value of each bit within the bit string of the first individual to the value of each bit within the bit string of the second individual. Support for these limitations can be found on page 7, lines 17-25 of Applicant's specification. Claims 17-19, 21, 22, and 29 are amended to provide proper antecedent basis for the claim language. Accordingly, no new matter is added by these amendments. For the reasons set forth below and the current amendments to the claims, Applicants respectfully request reconsideration of the present application.

***Claim Rejections Under 35 U.S.C. §112***

Claims 16-33 are rejected under 35 U.S.C. §112, 2<sup>nd</sup> paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner objects to the term "representative genomic microarray" as being vague and indefinite. Accordingly, Applicant has amended claims 16, 17, and 19 to replace the phrase "representative" with the term "reference," which is fully supported on page 7, line 11 of the specification. The Examiner is respectfully requested to reconsider and withdraw this rejection.

***Claim Rejections Under 35 U.S.C. §102 and §103***

Claims 16-25 and 32 are rejected as being anticipated by Gingeras et al, Salama et al., or Chee et al. pursuant to 35 U.S.C. §102(a), (b), or (e). Claims 16-25 are rejected as being anticipated by Eisen et al. pursuant to 35 U.S.C. §102(b). Claims 26-31 are rejected under 35



U.S.C. §103(a) as being unpatentable over Gingeras et al., Salama et al., or Chee et al., in view of Berno (U.S. Patent No. 6,223,127), while claim 33 is rejected under the same combination of references, and further in view of Applicant's admitted prior art. For the following reasons, Applicants respectfully request reconsideration and withdrawal each of these rejections.

### Applicant's Invention

By way of introduction, Applicant's invention is directed to a method for identifying and analyzing polymorphic markers in a population by genotyping individuals of the population to a fabricated reference microarray, then assigning a binary digit of 0 or 1 corresponding to the hybridization ratio for each segment within that microarray, resulting in a bit string for each individual that is genotyped. Each bit has a unique position (corresponding to a selected segment of the microarray) within the bit string, and the relationship of these unique positions within the bit string are consistent for every bit string that is generated for any of the individuals hybridized to the reference microarray. To determine the relatedness of the bit strings and to identify unique bits among a plurality of bit strings, the commonality of bit values at corresponding positions along the bit strings is evaluated to ascertain which bits are present and which bits are absent for any of the bit strings being compared.

### The Prior Art

Turning now to the prior art, none of the references cited by the Examiner in his Office Action (or in Applicant's specification) disclose or teach a method similar to that of the claimed invention. Gingeras et al., Salama et al., Chee et al., Eisen et al., and Berno are all directed to methods for the detection of polymorphisms in a population by hybridizing genomic DNA from an individual of a population to an array. Applicant admits that the problem of detecting polymorphisms in a population is well known. However, none of the cited references specifies the same methodology for determining this polymorphism that Applicant has disclosed and specifically claimed. In Applicant's invention, an algorithm is implemented which converts the hybridization ratio for each segment of the array into a binary digit of 0 or 1 to produce a bit string for each individual hybridized to the array. Each bit string generated has the same number of bits, and each bit has a unique position common to all the bit strings. To identify patterns of hybridization present in the population, the relatedness of the bit strings is determined by



comparing the value of each bit within the bit string of the first individual to the value of each bit within the bit string of the second individual, as claimed in independent 16.

In contrast to Applicant's claimed invention, the cited references use cluster analysis to determine relatedness of the hybridized individuals in a population. As best described in Berno (U.S. Patent No. 6,223,127) at col. 6, lines 10-55, cluster analysis is concerned with determining the closeness (i.e., the distances between segments) of hybridized segments and the number of groups of closely related segments that exist in the observed population. After all the distances are determined, an agglomerative hierarchical processing is implemented to group closely related (i.e., close in distance) genes so that a correlation or pattern, if any, can be ascertained. This process is not only significantly different but also significantly more complex than Applicant's method for determining relatedness. Applicant's claimed invention requires that entire bit strings be compared to one another, and the commonality and difference in value for each bit within the strings be determined. Specifically, the relatedness of the strings is determined by comparing the value of each bit within the bit string of the first individual to the value of each bit within the bit string of the second individual. By doing so, Applicant is able to provide a much simpler, more efficient process for observing the overall genetic profile of the individuals in a population. Since the entire genetic profile is observed, both mutations in the chromosomes of the populations of interest as well as the "noise" surrounding these markers (i.e., mutations in other chromosomes) can be ascertained. These features can be advantageous for evaluating the population in a phylogenetic context.

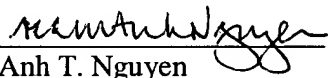
The cited references fail to teach or suggest all of the limitations of the claimed invention. For this reason, the presently pending claims are not anticipated or rendered obvious by any of these references, nor would their combination satisfy any deficiencies that might exist. This is because the specific method of the claimed invention is not disclosed or taught in *any* of the cited references. Accordingly, the Examiner is respectfully requested to reconsider and to withdraw these rejections.



In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

Dated: November 26, 2003

Respectfully submitted,

By   
Tram Anh T. Nguyen  
Registration No.: 47,257  
NUTTER MCCLENNEN & FISH LLP  
World Trade Center West  
155 Seaport Boulevard  
Boston, Massachusetts 02210-2604  
Tel: (617) 439-2734  
Fax: (617) 310-9734  
Attorneys for Applicant